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10/625,821	07/22/2003	Satoshi Mori	55022-DIV (71526)	7795

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EXAMINER

KUMAR, VINOD

ART UNIT PAPER NUMBER

1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/625,821

Applicant(s)

MORI ET AL.

Examiner

Vinod Kumar

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 July 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/645,825.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 8/20/03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-14 in the paper filed on March 5, 2007 is acknowledged. Claims 1-16 are pending.

Applicants argue that unity of inventions exists between Groups I and II (response, page 2, lines 6-9).

Applicant's argument was fully considered and was found to be persuasive. Accordingly, the restriction requirement is WITHDRAWN. Claims 1-16 are examined on merits in this Application.

Applicants are advised that if any claims including all the limitations of an allowable claim examined here are presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

2. An initialed and dated copy of Applicant's IDS form 1449 filed on 07/22/03 is attached to the instant Office action.

The listing of references in the specification (pages 21-22) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Priority

3. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy of Application No. Japan 10-96637/1998, filed 03/24/1998 has been received in the parent Application No. 09/646,825, filed on 09/22/2000.

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/646,825, filed 09/22/2000, now US Patent No. 6,849,724. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation,

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divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition

should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Drawings

4. The drawings are objected to because of the following informalities:

Drawings are objected to because they fail to comply with 37CFR 1.83.

In Figure 10, X-axis must be labeled.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet,

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and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Appropriate corrections are required.

Claim Objections

5. Claims 1, 4-5, 7, 9, and 10 are objected to because of following informalities:

In claim 1, line 2, replace "the" after "wherein" and before "region" with --a--.

In claim 1, line 3, replace "the" after "of" and before mRNA with --a--.

In claim 1, line 4, replace "the" after "of" and before "other" with --a--.

In claim 1, line 5, delete "the" at the end of claim.

In claim 1, line 6, replace "the" after "of" and before "protein" with --a--.

In claim 4, line 2, replace "the" after "from" and before "GT-rich" with --a--.

In claim 5, line 2, replace "a" after "of" and before "factor" with --the--.

In claim 7, line 3, insert --the--, after "of" and before "gene".

In claim 10, line 2, replace "nutrition" with --nutrients--.

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In claim 9, "Kozak sequence" must be referred to by its sequence identification number to comply with 37 CFR 1.821. There must not be any new matter submitted, therefore it is important to be careful to include only the sequences that are already disclosed in the current specification.

Appropriate action/corrections are required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2, 7, and 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in their recitation "gene" which is confusing since the limitation "gene" implies that the structure comprises the coding sequence and the associated promoter, terminator and enhancer encoding regions are also a part of the structure (see The Federal Register, Vol. 66, No. 4, Friday, January 5, 2001 at page 1108, left column, Endnote 13). In the instant case, Applicants do not appear to describe such gene associated nucleic acid sequences. It is suggested that "gene" be amended to "coding sequence". All subsequent recitations of "gene" are also rejected.

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Claim 1 and claims dependent thereon are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 1 is missing the essential step of expressing a modified gene from another species in a useful plant transformed with said modified gene.

Claims 1, 5, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in their recitation "gene of another species", which is confusing, since it is unclear whether the recitation includes or excludes the plants from the recitation. If the recitation includes other plant species, it is unclear why one skilled in the art would have to modify poly (A) region of said plant gene to practice the instantly claimed method. It is unclear what is intended?

Claims 1, 3, 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in their recitation "region of a factor" which is confusing since it is unclear which factor is being referred to? It is unclear what is intended?

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "substantially", which is confusing, since it is unclear what is intended? The recitation "substantially" is a relative term and has no definite meaning.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "derived", which is confusing, since it is unclear what is retained in the derived product.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "AATAAA like sequence", which is confusing since it is unclear which

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sequences are "AATAAA like" and which are not. It is unclear how an "AATAAA like" sequence is different from the "AATAAA" sequence. It is unclear what is intended? The metes and bounds of "like" are unclear and not defined...

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "reduced", which is confusing, since the recitation "reduced" is a relative term and has no definite meaning. The metes and bounds of the recitation are unclear as they are not defined.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "small difference", which is confusing, since the recitation "small difference" is a relative term and has no definite meaning. The metes and bounds of the recitation are unclear as they are not defined. It is unclear what is intended?

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "plant is seed" which is confusing since it is unclear how a plant can be a seed. A seed is a plant part not the plant. It is suggested to change "The plant according to claim 15, wherein the plant is seed" to --A seed produced by the plant of claim 15, and wherein said seed comprises said gene--.

Dependent claims 8, 13, and 14 are also rejected because they fail to overcome the deficiencies of claim 1.

Appropriate action/corrections are required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modified yeast FRE1 coding sequence as defined in SEQ ID NO: 1, a transgenic plant and a method of producing said transgenic plant comprising introducing and expressing said coding sequence in said transgenic plant, does not reasonably provide enablement for the scope of possible gene sequences from any species claimed for use in plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Claims are broadly drawn to a method for transforming a useful plant by introducing a gene of another species into the useful plant wherein the region of a factor relating to the poly (A) addition of the mRNA of the useful plant to be transformed contained in the base sequence of the gene of the other species is modified into

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another base sequence not relating to the poly (A) addition of the mRNA without substantially altering the function of the protein, or wherein the gene is derived from yeast, or wherein the region of a factor relating to the poly (A) addition of the mRNA is a base sequence having AATAAA like sequence, or wherein region of a factor relating to the poly (A) addition of the mRNA is located in a downstream from the GT-rich base sequence, or wherein the modification of base sequence in the region of a factor relating to the poly (A) addition of the mRNA is performed based on a codon usage of the useful higher plant, or wherein the modification of base sequence is performed so that the region rich in base G and base T is reduced, or wherein the modification of base sequence comprises small difference between base G and base C covering throughout the region of the gene to be introduced, or wherein the modification of base sequence is performed so as to have ATTTA sequence, or wherein Kozak sequence is present in the upstream of the initiation codon of the gene to be introduced, or wherein the gene to be introduced encodes a protein involved in absorption of nutrition, or wherein introduced gene encodes ferric-chelate reductase FRE1, or wherein gene encoding ferric-chelate reductase FRE1 is derived from yeast, or wherein useful plant is grass or tobacco, or a transgenic plant or transgenic seed produced by said method.

The specification as filed teaches making modifications of the yeast FRE1, specifically making instant SEQ ID NO: 1, for use in plants. The specification teaches transgenic tobacco plants expressing modified yeast FRE1. The transgenic plants expressing modified yeast FRE1 exhibited functional enzymatic activity. See Figures 1-

18; pages 22-37, Examples 1-9. Transgenic plants expressing any other modified gene sequences obtained from a different species are not taught.

Claim 1 is directed to any gene from any species that can be modified in a region of a factor relating to the poly (A) addition of a mRNA of any useful plant, and wherein said modification comprises changing the base sequence to a sequence which is not related to the poly (A) addition of the mRNA of said useful plant. Claim 3 limits the sequence to be modified to AATAAA like sequence, and claim 4 limits said region to any downstream position from any GT-rich base sequence. The claims encompass any possible nucleic acid gene sequences having any such modifications of a downstream area of a GT-region by replacing any "region of a factor relating to the poly (A) addition of the mRNA.

The breadth of any nucleic acid claimed rests on negative limitations so that Applicants claim any nucleic acid sequence which potentially has the described "region of a factor relating to the poly(A) addition of the mRNA" in any gene presumably from foreign genes not normally expressed in plants and/or not having the specific regions claimed. The specification as filed does not provide any other example genes which would require such modification other than the yeast FRE1 gene for expression in tobacco. Plant polyadenylation signals do not have a strict consensus requirement. For example, see Grec et al. (Gene 242, 87-95, 2000) who teach cryptic polyadenylation sites within the coding sequences of PDR5 (pleiotropic drug resistance) and MIP (mitochondrial DNA polymerase) genes expressed in tobacco. No AATAAA related

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elements were found upstream of the cryptic poly A sites of PDR5 or MIP genes expressed in tobacco.

Therefore, other than a vague teaching to look for GT-rich areas in any such gene, and change the sequence to remove certain sequences, one of skill in the art would not immediately envision on what is otherwise any possible nucleic acid gene sequence as broadly claimed. The art indicates (e.g. Grec et al.) that the structure of nucleic acid sequences, i.e. any gene for instance, is empirically determined and the structural elements of a gene in one species will have different regulatory sequences and different structural elements. There would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO: 1 do not provide a substantial correlation to any such modification needed or required in any other nucleic acid sequence broadly claimed.

Claim 1 and claims dependent thereon are directed to a coding sequence comprising substitutions, additions, and deletions of one or more nucleotides due to the modifications in the coding sequence. This implies that the encoded protein derived from said modified sequence would comprise addition, substitutions or deletions of one or more amino acids when compared with its naturally occurring counterpart. While it is known that many amino acid substitutions, additions or deletions are generally possible in any given protein the positions within the protein's sequence where such amino acid

changes can be made with a reasonable expectation of success (without altering protein function) are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see for example, Wells, *Biochemistry* 29:8509-8517, 1990, Applicant's IDS; Ngo et al., pp. 492-495, 1994, Applicant's IDS). Furthermore, Keskin et al. (*Protein Science*, 13:1043-1055, 2004) teach that proteins with similar structure may have different functions. Besides, Thornton et al. (*Nature structural Biology*, structural genomics supplement, November 2000) teach that structural data may carry information about the biochemical function of the protein. It's biological role in the cell or organism is much more complex and actual experimentation is needed to elucidate actual biological function under *in vivo* conditions. Furthermore, Guo et al. (*PNAS*, 101: 9205-9210, 2004) teach that there is a probability factor of 34% that a random amino acid replacement in a given protein will lead to its functional inactivation. In the instant case, modifying the GC/GT content of the transcript would encompass more than single amino acid change in the encoded protein. Neither the state of art nor Applicants provide guidance as to how inoperable embodiments can be readily eliminated other than random trial and error. The additions, deletions or substitutions in one or more amino acid residues would also encompass changes in the functionally important domain(s) of the encoded protein. In the absence of guidance, undue experimentation would have been required by a skilled artisan at the time

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claimed invention was made to determine how to modify the region of a factor relating to the poly (A) addition of the mRNA into another sequence not related to the poly(A) addition of the mRNA and/or changing GC/GT content in said "region of a factor" without altering the function of the encoded protein. See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification, as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention. Therefore, it is maintained that the claimed invention is not enabled as commensurate in scope with the claims.

8. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are broadly drawn to a method for transforming a useful plant by introducing a gene of another species into the useful plant wherein the region of a factor relating to the poly (A) addition of the mRNA of the useful plant to be transformed contained in the base sequence of the gene of the other species is modified into another base sequence not relating to the poly (A) addition of the mRNA without substantially altering the function of the protein, or wherein the gene is derived from

yeast, or wherein the region of a factor relating to the poly (A) addition of the mRNA is a base sequence having AATAAA like sequence, or wherein region of a factor relating to the poly (A) addition of the mRNA is located in a downstream from the GT-rich base sequence, or wherein the modification of base sequence in the region of a factor relating to the poly (A) addition of the mRNA is performed based on a codon usage of the useful higher plant, or wherein the modification of base sequence is performed so that the region rich in base G and base T is reduced, or wherein the modification of base sequence comprises small difference between base G and base C covering throughout the region of the gene to be introduced, or wherein the modification of base sequence is performed so as to have ATTTA sequence, or wherein Kozak sequence is present in the upstream of the initiation codon of the gene to be introduced, or wherein the gene to be introduced encodes a protein involved in absorption of nutrition, or wherein introduced gene encodes ferric-chelate reductase FRE1, or wherein gene encoding ferric-chelate reductase FRE1 is derived from yeast, or wherein useful plant is grass or tobacco, or a transgenic plant or transgenic seed produced by said method.

The specification as filed describes making modifications of the yeast FRE1, specifically making instant SEQ ID NO: 1, for use in plants. The specification describes transgenic tobacco plants expressing modified yeast FRE1. The transgenic plants expressing modified yeast FRE1 exhibited functional enzymatic activity. See Figures 1-18; pages 22-37, Examples 1-9. Transgenic plants expressing any other modified gene sequences obtained from a different species are not described.

Claim 1 is directed to any gene from any species that can be modified in a region of a factor relating to the poly (A) addition of the mRNA of the any useful plant, and wherein said modification comprises changing the base sequence to a sequence which is not related to the poly (A) addition of the mRNA of said useful plant. Claim 3 limits the sequence to be modified to AATAAA like sequence, and claim 4 limits said region to any downstream position from any GT-rich base sequence. The claims encompass any possible nucleic acid gene sequences having any such modifications of a downstream area of a GT-region by replacing any "region of a factor relating to the poly (A) addition of the mRNA. Claim 10 is directed to any gene sequence from any source involved in absorption of nutrients. Claim 11 encompasses any modification in poly (A) region of ferric-chelate reductase FER1 derived from any source. Claim 12 is directed to any modification in poly(A) region of any ferric-chelate reductase FRE1 derived from yeast.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and

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that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Id.*

See also MPEP Section 2163, page 174 of Chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

The specification does not have adequate written description for genus of nucleic acid sequences comprising a coding sequence which has been modified to encode a functionally unaltered protein. It was not clear at the time the invention was made that Applicant was in possession of a representative number of species of any modified nucleic acid sequence as broadly claimed. The art indicates that the structure of nucleic acid sequences, i.e. any gene for instance, is empirically determined and the

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structural elements of a gene in one species will have different regulatory sequences and different structural elements. There would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO: 1 do not provide a substantial correlation to any such modification needed or required in any other nucleic acid sequence broadly claimed. One of skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claims.

The breadth of any nucleic acid claimed rests on negative limitations so that Applicants claim any nucleic acid sequence which potentially has the omission of certain GT rich regions and sequences encoded by an AATAAA or ATTTA region. The specification as filed does not provide any other example genes which would require such modification other than the yeast FRE1 gene for expression in tobacco. There would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO:1 do not provide a substantial correlation to any such modification needed or required in any other nucleic acid sequence broadly claimed. One of skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of only one

member of this genus is not representative of the variants of the genus and is insufficient to support the claims.

Furthermore, MPEP 608.01(p) states that Essential material "is defined as that which is necessary to (1) describe the claimed invention..." and such essential material may not be incorporated by reference into the instant specification as filed. It would be essential to know other starting gene sequences which would be applicable to the instantly claimed modifications in order to show that applicant was in possession of a representative number of species of such template sequences at the time the invention was made.

Claim 6 requires that the base sequence is optimized such that G+T content is reduced in the region of modification. However, neither the specification nor the prior art described an art recognized definition for what a "reduced amount" of G+T content looks like in the region of modification. As such, applicant has not clearly described the claimed invention such that one of skill in the art would have recognized that applicant was in possession of a representative number of species of any gene sequence having the optimized consistent use of G+T content since no standard level or placement of G+T content is defined in the specification as filed or the prior art.

Claim 7 requires that the base sequence is optimized such that G+C content is different throughout the region of a gene. However, neither the specification nor the prior art described an art recognized definition for what a "small difference" in G+C content looks like in the entire region of a gene. The art recognizes that G+C content is found in a certain percentage in a gene sequence, but does not further specify the

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amount, nor the placement of the G and C sequences that is considered "consistent" for any possible gene sequence. As such, applicant has not clearly described the claimed invention such that one of skill in the art would have recognized that applicant was in possession of a representative number of species of any gene sequence having the optimized consistent use of G+C content since no standard level or placement of G+C content is defined in the specification as filed or the prior art.

Specification does not describe these undisclosed structures of Applicant's broadly claimed genus and one skilled in the art cannot reliably predict the structure of these sequences based upon the disclosure of SEQ ID NO: 1. Furthermore, said structures of Applicant's broadly claimed genus are not correlated to the function of preventing cryptic polyadenylation and producing functional protein in a transgenic plant. Further, Applicants have failed to describe conserved functional domains that are shared by these undisclosed structures of their broadly claimed genus. Applicants have failed to reduce their broadly claimed genus to practice.

Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide written description of the genus broadly claimed. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 3-5, 7-8, 14, 15 and 16 are rejected under 35 U.S.C. 102(b) as anticipated by Perlak et al. (PNAS, 88:3324-3328, April 1991, Applicant's IDS).

Perlak et al. disclose a method of making a transgenic plant and seeds derived thereof comprising introducing and expressing a modified coding sequence *cryIA(b)* gene of *Bacillus thuringiensis* in transgenic tobacco and tomato plants. The transgenic plants exhibited improved insect resistance. The modification did not alter the amino acid sequence of the CryIA(b) protein. The modification of coding sequence for *cryIA(b)* comprised altering AATAAA and/or ATTTA sequences. Furthermore, the modification increased (increase is encompassed by difference) G and C content throughout the region of gene to be introduced, and modification was based on plant preferred codons without changing the amino acid sequence. See in particular, page 3324, abstract; page 3324, 2nd paragraph, materials and methods (modification of the coding sequence of insect control genes) through the end of 2nd paragraph of 1st column of page 3325; page 3325, Table 1; page 3326, Figure 1, Table 2; page 3327, Figure 2, Table 3; Page 3328, 1st column, discussion.

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Accordingly, Perlak et al. anticipated the claimed invention.

10. Claims 1, 5, 7-8, 13, 15, and 16 are rejected under 35 U.S.C. 102(b) as anticipated by Nayak et al. (PNAS, 94:2111-2116, March 1997).

Nayak et al. disclose a method of making a transgenic plant and seeds derived thereof comprising introducing and expressing a modified coding sequence *cryIAc* gene of *Bacillus thuringiensis* in transgenic rice (grass) plants. The transgenic plant exhibited improved insect resistance. The modification did not alter the amino acid sequence of the CryIAc protein. The modification of coding sequence for *cryIAc* comprised altering ATTTA sequences. Furthermore, the modification increased (increase is encompassed by difference) G and C content throughout the region of gene to be introduced, and modification was based on plant preferred codons without changing the amino acid sequence. See in particular, page 2111, abstract; page 2113, figure 3, table 1; page 2114, figures 4-6, table 2; page 2115, 2nd column, figures 7 and 8;.

Accordingly, Nayak et al. anticipated the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Perlak et al. (PNAS, 88:3324-3328, April 1991) in view of Kozak (Nucleic Acids Research, 9:5233-5252, 1981).

Perlak et al. teach a method of making a transgenic plant and seeds derived thereof comprising introducing and expressing a modified coding sequence *cryIA(b)* gene of *Bacillus thuringiensis* in transgenic tobacco and tomato plants. The transgenic plants exhibited improved insect resistance. The modification did not alter the amino acid sequence of the CryIA(b) protein. The modification of coding sequence for *cryIA(b)* comprised altering AATAAA and/or ATTTA sequences. Furthermore, the modification increased (increase is encompassed by difference) G and C content throughout the region of gene to be introduced, and modification was based on plant preferred codons without changing the amino acid sequence. See in particular, page 3324, abstract; page 3324, 2nd paragraph, materials and methods (modification of the coding sequence of insect control genes) through the end of 2nd paragraph of 1st column of page 3325; page 3325, Table 1; page 3326, Figure 1, Table 2; page 3327, Figure 2, Table 3; Page 3328, 1st column, discussion.

Perlak et al. do not teach Kozak sequence.

Kozak teach that Kozak sequence(s) increases the efficiency of binding of an eukaryotic mRNA to ribosome(s) and thus increasing the efficiency of translation initiation during protein synthesis. See in particular, page 5233, abstract; pages 5234-5236; page 5237, figure 1; table 1; page 5242, table 2, figure 2; page 5347-5249.

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It would have been obvious for one of the ordinary skill in the art at the time the claimed invention was made to modify Perlak et al. method for transforming a useful plant by adding a step of inserting Kozak sequence to the 5' end of translation initiation codon "AUG" in bacterial *cryIA(b)* gene sequence. Given that *cryIA(b)* gene sequence is derived from a bacteria, and Kozak teach that "Kozak sequence" increases the binding efficiency of a mRNA to the eukaryotic ribosome(s), one of ordinary skill in the art would have been motivated at the time the claimed invention was made to insert Kozak sequence(s) in Perlak et al. gene sequence for increasing the efficiency of translation initiation of *cryIA(b)* mRNA transcripts expressed in a plant to produce an insect resistant transgenic plant with reasonable expectation of success.

Thus, the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

Conclusions

12. Claims 1-16 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

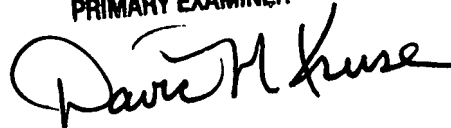
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Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVID H. KRUSE, PH.D.
PRIMARY EXAMINER

A handwritten signature in black ink that reads "David H. Kruse". The signature is written in a cursive style with a large, looped "D" and a stylized "K".